

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 15:44:22 ON 15 JUL 2003

=> file medline caplus biosis

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'MEDLINE' ENTERED AT 15:44:34 ON 15 JUL 2003

FILE 'CAPLUS' ENTERED AT 15:44:34 ON 15 JUL 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 15:44:34 ON 15 JUL 2003

COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

=> protease activated receptor

L1 1727 PROTEASE ACTIVATED RECEPTOR

=> broncho?

L2 168008 BRONCHO?

=> l1 and l2

L3 37 L1 AND L2

=> l3 and 1970-1999/py

L4 7 L3 AND 1970-1999/PY

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 3 DUP REM L4 (4 DUPLICATES REMOVED)

=> d ti abs so l5 1-3

L5 ANSWER 1 OF 3 MEDLINE

DUPLICATE 1

TI A protective role for **protease-activated receptors** in the airways.

AB The protection of cells in the upper intestine against digestion by pancreatic trypsin depends on the prostanoid prostaglandin E2 (PGE2) and is mediated by **protease-activated receptors** in the epithelium. As the airway epithelium is morphologically similar and also expresses one of these receptors, PAR2, and is a major source of PGE2, we reasoned that bronchial epithelial PAR2 might also participate in prostanoid-dependent cytoprotection in the airways. Here we show that activation of PAR2, which co-localizes immunohistochemically with trypsin(ogen) in airway epithelium, causes the relaxation of airway preparations from mouse, rat, guinea-pig and humans by the release of a cyclooxygenase product from the epithelium. This physiological protective response in isolated airways also occurred in anaesthetized rats, where activation of PAR2 caused a marked and prolonged inhibition of **bronchoconstriction**. After desensitization of PAR2, the response to trypsin recovered rapidly by mechanisms dependent on de novo synthesis and trafficking of proteins. Our results indicate that trypsin released from the epithelium can initiate powerful **bronchoprotection** in the airways by activation of epithelial PAR2.

SO NATURE, (1999 Mar 11) 398 (6723) 156-60.

Journal code: 0410462. ISSN: 0028-0836.

L5 ANSWER 2 OF 3 MEDLINE

DUPLICATE 2

TI alpha-Thrombin stimulates contraction of human bronchial rings by activation of **protease-activated receptors**.

AB In a variety of diseases, inflammation causes microvascular leakage and

activates thrombin. Evidence suggests that thrombin increases cytosolic calcium and stimulates human airway smooth muscle (ASM) cell proliferation. The receptor subtypes, however, that mediate the effects of thrombin on ASM cell growth or calcium mobilization remain unknown. In this study, we postulate that thrombin, which activates specific **protease-activated receptors** (PARs), also stimulates contraction of isolated human bronchial rings. With the use of intact human bronchial rings, alpha-thrombin (1-20 U/ml) increased bronchial tone to 19 +/- 3% of basal tone (P = 0.008; n = 5 experiments) and represents 20 +/- 8% of the maximum carbachol response. The EC(50) for thrombin-induced force generation was 12.2 U/ml (95% confidence interval 9.9-15.3 U/ml) and was not altered in bronchial rings that had the epithelium removed. In parallel experiments, a specific thrombin receptor-activating peptide (TRAP-14; 0.1-100 micromol/l) increased isometric tension to levels (14 +/- 2%; P = 0.0005; n = 5 experiments) comparable to those rings stimulated with thrombin. To characterize the receptors that mediate thrombin effects on human ASM, the expression of PARs in cultured human ASM cells was analyzed by RT-PCR analysis with specific primers for PARs. In these cells, PAR1 (thrombin receptor), PAR2, and PAR3 were expressed at comparable levels. In other experiments using immunocytochemical staining with specific antibodies to PAR1 and PAR2, we showed that ASM in bronchial rings and cultured ASM cells express PAR1 and PAR2 proteins. Taken together, these studies suggest that alpha-thrombin, in a receptor-specific and dose-dependent manner, induces contraction of bronchial rings in vitro. In addition, cultured human ASM cells express mRNA of PAR1, PAR2, and PAR3 and express PAR1 and PAR2 protein. Further studies are needed to determine whether alpha-thrombin plays a role in stimulating **bronchoconstriction** in inflammatory airway diseases such as asthma and bronchiolitis obliterans.

SO AMERICAN JOURNAL OF PHYSIOLOGY, (1999 Jul) 277 (1 Pt 1) L22-9.
Journal code: 0370511. ISSN: 0002-9513.

L5 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

TI A role for thrombin and proteinase-activated receptor 1 (PAR1) in guinea-pig **bronchospasm**.

SO British Journal of Pharmacology, (Oct., 1997) Vol. 122, No. PROC. SUPPL., pp. 14P.

Meeting Info.: Proceedings of the British Pharmacological Society Meeting Bristol, England, UK July 23-25, 1997 British Pharmacological Society . ISSN: 0007-1188.

=> d au 15 1-3

L5 ANSWER 1 OF 3 MEDLINE

DUPLICATE 1

AU Cocks T M; Fong B; Chow J M; Anderson G P; Frauman A G; Goldie R G; Henry P J; Carr M J; Hamilton J R; Moffatt J D

L5 ANSWER 2 OF 3 MEDLINE

DUPLICATE 2

AU Hauck R W; Schulz C; Schomig A; Hoffman R K; Panettieri R A Jr

L5 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AU Cicala, C. (1); Bucci, M. (1); De Dominicis, G.; Cirino, G.

=> thomas?/au and cocks?/au

L6 20 THOMAS?/AU AND COCKS?/AU

=> james?/au and moffett?/au

L7 1 JAMES?/AU AND MOFFETT?/AU

=> d his

(FILE 'HOME' ENTERED AT 15:44:22 ON 15 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 15:44:34 ON 15 JUL 2003

L1 1727 PROTEASE ACTIVATED RECEPTOR
L2 168008 BRONCHO?
L3 37 L1 AND L2
L4 7 L3 AND 1970-1999/PY
L5 3 DUP REM L4 (4 DUPLICATES REMOVED)
L6 20 THOMAS?/AU AND COCKS?/AU
L7 1 JAMES?/AU AND MOFFETT?/AU
L8 0 L6 AND L1
L9 0 L7 AND L1

=> logoff